REMARKS

Claims 25-30 were pending in the application. Claim 25 has been amended. Upon entry of these amendments, Claims 25-30 will be pending and under active consideration. Claim 25 is independent.

Applicants submit respectfully that the amendments presented herein are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter.

Claim 25 has been amended to point out more particularly and claim more distinctly that which Applicants regard as their invention by now no longer reciting "or a serine protease inhibitor" and reciting instead "(benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide." Claim 25 has additionally been amended to recite "and a therapeutically effective amount of at least one free radical scavenger, wherein the at least one free radical scavenger is 2,6,8-trihydroxypurine, dihydrorhodamine, or a combination thereof". The amendments are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

I. The Rejection Under Obviousness Type Double Patenting Should Be Held In Abeyance

The Office Action, at page 2, provisionally rejects Claims 25 and 28 as allegedly being unpatentable over claims 34-36 of copending application number 10/427,929 under the doctrine of nonstatutory obviousness-type double patenting.

Without acquiescing in the propriety of the rejection and solely to advance the prosecution of the present application, Applicant respectfully requests that the obviousness-type double patenting rejection be held in abeyance until an indication of allowable subject matter is received.

II. Rejections Under 35 U.S.C. § 112, First Paragraph

At page 3 of the Office Action, Claims 25-30 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention, for the reasons of record. The reasons of record, in sum, allege that while the specification is enabling for treating septic shock, induced inflammation and endotoxemia with the administration of (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide, does not reasonably provide enablement for treating ischemia reperfusion injury; the additional administration of a thrombolytic agent, and the additional use of a mechanical device to reestablish blood flow, the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

and/or use the invention commensurate in scope with these claims.. Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, Claim 25 is amended herein to delete reference to "or a serine protease inhibitor" and substitute therefore "(benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide." Applicant has additionally amended Claim 25 herein to now also recite that "and a therapeutically effective amount of at least one free radical scavenger, wherein the at least one free radical scavenger is 2,6,8-trihydroxypurine, dihydrorhodamine, or a combination thereof".

Applicant respectfully submits that the specification as filed clearly provides the teaching necessary to adequately supports the enablement of Claims 25-30 as amended herein without undue experimentation. In particular, the specification recites at page 22, lines 28-31 that [t]he combination of a serine protease inhibitor and/or NO inhibitory agent with tPA, streptokinase, and the like, can reduce inflammation and NO production and apoptosis associated with infarct because NO and free radical production occur during ischemia/reperfusion."

On this basis, Applicants submit respectfully that the rejection for alleged undue breadth of the claim has been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, first paragraph, rejection of Claims 25-30 be withdrawn.

II. The Rejections Under 35 U.S.C. § 102(b) Should Be Withdrawn

At page 6 of the Office Action, Claims 25 and 28 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by are rejected under 35 U.S.C. 102(b) as being anticipated by Gyorkos et al. (U.S. Patent No. 5,618, 792). The Office Action asserts that Gyorkos et al. teach substituted oxadiazole, thiadiazole and triazole peptoids, which are useful as inhibitors of serine proteases including human neutrophil elastase (elastase inhibitory activity) and Column 7, lines 45-57 teaches the instant compounds that are used to treat various diseases such as ischemia/reperfusion or other conditions disclosed in column 1, lines 28-42. Applicants traverse respectfully.

Applicants submit respectfully that Claim , as amended, is not anticipated by because Gyorkos et al. does not disclose each and every element of those amended claims as is required for a *prima facie* showing of anticipation. In particular, Claim , as amended, is directed to a method of treating ischemia reperfusion injury, comprising administering at least one of alpha1-antitrypsin, alpha1-antitrypsin-like agent, antielastase, or antiproteinase-3 agent, (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide, or a combination thereof, and a therapeutically effective amount of at least one free radical scavenger, wherein the at least one free radical scavenger is 2,6,8-trihydroxypurine, dihydrorhodamine, or a combination thereof. Applicants submit respectfully that Gyorkos et al. does not teach or suggest a method of treating ischemia reperfusion injury, comprising administering at least one of alpha1-antitrypsin, alpha1-antitrypsin-like agent, antielastase, or antiproteinase-3 agent, (benzyloxycarbonyl)-L-valyl-N-[1-(3-

(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide, or a combination thereof, and a therapeutically effective amount of at least one free radical scavenger, wherein the at least one free radical scavenger is 2,6,8-trihydroxypurine, dihydrorhodamine, or a combination thereof.

Applicant submits respectfully that the claims of the present invention, as amended, are not anticipated by Gyorkos et al. and that the rejection of Claims 25 and 28 under 35 U.S.C. § 102(b) has been overcome. Accordingly, Applicant requests respectfully that the rejection of Claims 25 and 28 under 35 U.S.C. § 102(b) be withdrawn.

III. The Rejections Under 35 U.S.C. § 103(a) Should Be Withdrawn

The Office Action, at pages 7-8, rejects Claims 25-28 and 30 as allegedly being obvious over Gyorkos et al. (U.S. Patent No. 5,618, 792) (hereinafter, "Gyorkos et al."), under 35 U.S.C. § 103(a) Claims 25-28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gyorkos et al. (5,618,792) in view of Verstraete, "Intravenous administration of a thrombolytic agent is the only realistic therapeutic approach in evolving myocardial infarction", European Heart Journal, Vol. 6, pp. 586-593 (1985) and further in view of woods (5,180, 366), and further in view of woods (5,180, 366). The Office Action alleges that Gyorkos et al. teaches the use of (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2=(S)-methylpropyl]-L-prolinamide to treat ischemia reperfusion injury, and that while the instant invention differs from the cited reference in that the cited reference does not teach the addition of a second agent, a thrombolytic agent as

disclosed in claim 26, the secondary reference, Verstraete, teaches a thrombolytic agent such as streptokinase to treat myocardial infarction, an ischemia reperfusion injury. The Office Action is of the opinion that one skilled in the art would have assumed to combination of two individual agents know to treat ischemia reperfusion injuries into a single composition would give an additive effect in the absence of evidence to the contrary. Applicants traverse respectfully.

Applicant submits respectfully that Claim 25 as amended herein directed to a method of treating ischemia reperfusion injury, comprising administering at least one of alpha1-antitrypsin, alpha1-antitrypsin-like agent, antielastase, or antiproteinase-3 agent, (benzyloxycarbonyl)-L-valyl-N-[1-(3-(5-(3-trifluoromethylbenzyl)-1,2,4-oxadiazolyl)carbonyl-2-(5)-methylpropyl]-L-prolinamide, or a combination thereof, and a therapeutically effective amount of at least one free radical scavenger, wherein the at least one free radical scavenger is 2,6,8-trihydroxypurine, dihydrorhodamine, or a combination thereof is neither taught nor suggested by the primary reference of Gyorkos et al., taken either alone or in combination with either secondary reference of Verstraete or Woods et al. Thus, Applicants submit respectfully that, as neither Verstraete nor Woods cure the deficiencies of Gyorkos et al. with respect to Claims 25-28 and 30 of the present invention, the combination of the Cited References fails to meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

Accordingly, Applicants submit respectfully that the rejection of Claims 25-28 and 30 under 35 U.S.C. § 103(a) have been overcome, and Applicants request respectfully that the rejection of Claims 25-28 and 30 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicant submits respectfully that the present application is in condition for allowance. Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office Action, and an early Notice of Allowance are requested.

Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 373-6122.

AUTHORIZATION

Applicants believe there is no fee due in connection with this filing. However, to the extent required, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 19-5127 (**7049795003**) or credit any overpayment to same.

Dated: August 17, 2006

Respectfully submitted,

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